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Title: Is BMI higher in younger patients with COVID-19? Association between BMI and COVID-19 hospitalization by age

Running Title: BMI higher in young patients with COVID-19

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What is already known about this subject?

1. The novel Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) has created a pandemic globally with its syndrome COVID-19.
2. Obesity has recently been shown to be a risk factor for hospitalization for patients with COVID-19.

What are the new findings in your manuscript?

1. Our findings suggest that younger patients (age < 50 years) hospitalized with COVID-19 have a higher BMI than older patients (age ≥ 50 years) hospitalized with COVID-19, and this remains true in subgroups of patients without diabetes and hypertension.
2. Our findings demonstrate a negative correlation of BMI and age for patients hospitalized with COVID-19, suggesting degree of obesity matters relative to age (not observed in patients without COVID-19).

How might your results change the direction of research or the focus of clinical practice?

1. For those hospitalized with COVID-19, additional attention needs to be paid to BMI, especially with young patients.
2. Weight-related medical conditions may play a role in more severe COVID-19 and require further study.

Abstract

Objective: Obesity has been found to be a risk factor for hospitalization with COVID-19. We were interested in understanding whether patients hospitalized with COVID-19 differed in BMI at older versus younger ages, and if trends were independent of diabetes and hypertension.

Methods: We performed a cross-sectional analysis of patients hospitalized with moderate to severe COVID-19 at Northwestern Memorial Hospital from March 19th, 2020 until April 4th, 2020. We compared patients hospitalized with COVID-19 above and below the age of 50, and to those hospitalized without COVID-19.

Results: We found patients younger than 50 years of age hospitalized with COVID-19 without diabetes or hypertension had mean BMI greater than those older than 50 years of age, with BMI 43.1 (95%CI 34.5 – 51.7) kg/m² vs 30.1 (95%CI 27.7 – 32.5) kg/m² (p=0.02). Furthermore, BMI appears to inversely correlate with increasing age amongst patients hospitalized with COVID-19. We did not detect the same difference or trend for patients hospitalized without COVID-19.

Conclusion: We found younger patients (age <50 years) with COVID-19 had higher mean BMI than older patients with COVID-19, with and without diabetes and hypertension. This trend did not exist in patients without COVID-19 hospitalized during the same time-period.

Introduction

The novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and its clinical syndrome, COVID-19, pose a major risk for the population and healthcare institutions. The Center for Disease Control (CDC) lists severe obesity [Body Mass Index (BMI) $\geq 40\text{kg/m}^2$] as a risk factor for COVID-19. Recent studies suggest obesity is a risk factor for hospitalization of patients younger than 60 years with COVID-19.¹ Increased BMI is associated with progression to more severe COVID-19.² Hypertension and Type 2 diabetes (DM), two obesity related co-morbidities and components of the metabolic syndrome, are associated with poor outcomes of COVID-19.³ No studies have evaluated BMI as a function of age while controlling for DM and hypertension for patients hospitalized with COVID-19. We were interested in understanding whether patients hospitalized with COVID-19 differed in BMI at older versus younger ages, and among subgroups with and without DM and hypertension. We hypothesized that patients hospitalized with COVID-19 have higher BMI than those hospitalized without COVID-19, irrespective of DM and hypertension.

Methods

We performed a cross-sectional study of patients hospitalized at Northwestern Memorial Hospital, an 894-bed tertiary medical center located in downtown Chicago, Illinois. We included all hospitalized adults (age greater than 18 years) from March 19th, 2020 until April 4th, 2020. We defined patients with COVID-19 as patients hospitalized for moderate to severe COVID-19 symptoms (fever, cough, and dyspnea) and SARS-CoV-2 infection confirmed by RT-PCR. We defined patients without COVID-19 as patients hospitalized for any reason other than COVID-19. Patients were tested only if symptomatic, in accordance with CDC, national, and local guidelines at the time. Patients were tested using kits provided by the CDC, the local public health department, or Emergency Use Authorized assays, the only available tests at the time. We reviewed the electronic medical record (EMR) and enterprise data warehouse (EDW) for our population of interest. BMI was defined as first BMI value listed in the EDW and/or EMR, on or after admission. We did not consider any patients without listed weight or height as BMI was not defined. A patient was considered to have hypertension if the diagnosis was listed in the EMR problem list. A patient was considered to have DM if listed on the problem list or if an available hemoglobin A1c result was $\geq 6.5\%$. Patients without any hemoglobin A1c result or diabetes problem notation were classified as "DM-unknown." We excluded patients discharged directly from the Emergency Department (ED) and patients who were pregnant. We compared patients above

and below the age of 50 years with and without COVID-19. We chose this age because studies suggest mortality for patients with COVID-19 increases significantly for those age 50 years and older.⁴ Two sample t-test was used to compare BMI between age groups. To evaluate the association between age and BMI, linear regression was fit by regressing BMI on age, COVID-19 status, and an interaction term between age and COVID-19 status. Analysis was conducted first on all hospitalized patients by age above and below 50, then on patients without hypertension but with DM-unknown, finally patients without hypertension and without DM. Analyses were conducted using SAS version 9.4 (Cary, NC). The study was approved by the Northwestern IRB.

Results

During the period of study, 227 patients were hospitalized with COVID-19 and 183 were hospitalized without COVID-19. Characteristics were similar between groups, with exception of higher rates of hypertension in those hospitalized with COVID-19 (49% vs 35%). Remainder of characteristics are listed in Table 1.

In all patients hospitalized with COVID-19, mean BMI for those younger than 50 years of age was greater than those over 50 years of age, 34.2 (95%CI 32.1 – 36.3) kg/m² vs 29.9 (95%CI 28.8 – 31.0) kg/m² (p=0.0006). In the subset without DM or hypertension, mean BMI for those younger than 50 years of age was greater than those over 50 years of age, 43.1 (95%CI 34.5 – 51.7) kg/m² vs 30.1 (95%CI 27.7 – 32.5) kg/m² (p=0.02). In the subset without hypertension but with DM-unknown, a similar numerical trend followed with mean BMI greater in younger patients, 31.9 (95%CI 29.7 – 34.1) kg/m² vs 28.8 (95%CI 26.4 – 31.2) kg/m² (p=0.06), but results were not statistically significant.

Mean BMI for all patients hospitalized with COVID-19 was 31.2 (95%CI 30.2 – 32.3) kg/m², above the threshold for class I obesity. Mean BMI for all hospitalized patients without COVID-19 was BMI 28.1 (95%CI 27.0 – 29.3) kg/m², classified as overweight. The difference between the two groups was statistically significant (p=0.0001).

No differences in BMI were found between groups for hospitalized patients without COVID-19, with exception that those over 50 years of age had higher BMI than those under 50 years of age when without DM or hypertension (the opposite of the COVID-19 trend). Results are listed in Table 2.

Figure 1 demonstrates the trend of BMI with age for all patients hospitalized with and without COVID-19. Patients with COVID-19 were 20-91 years of age. Patients without COVID-19 were 18-96 years of age.

Discussion

In this cross-sectional study, patients less than 50 years old hospitalized with COVID-19 had significantly higher mean BMI and were more likely to have a higher class of obesity than patients over 50 years of age. Interestingly, BMI appears to decrease with increasing age among patients hospitalized with COVID-19, and in subgroups without DM or hypertension. We did not observe the same associations between BMI and age for hospitalized patients without COVID-19. Our findings suggest obesity, and degree of obesity, might be particularly important among those less than 50 years old hospitalized with COVID-19. Further research is needed to understand if obesity, or degree of obesity, in relation to age, is an independent risk factor for COVID-19 disease progression requiring hospitalization, ICU care, and intubation. Notably, mean BMI for our patients in most groups was lower than the at-risk value of 40kg/m^2 as specified by the CDC. It may be prudent to study all patients with $\text{BMI} \geq 30\text{kg/m}^2$ (class I obesity) for future analyses, as other sources seem to have similar trends.¹ One study classified obesity as $\text{BMI} \geq 28\text{kg/m}^2$,² though this would be in the category of overweight by our classifications.

Reasons for this association are unclear. Obesity has been linked to a constitutionally active inflammatory and prothrombotic state.^{5,6} A predisposition for inflammation and thrombosis could potentially explain our observations. Anecdotally, inflammatory markers rise considerably in COVID-19 and thrombosis is noted to be common. Younger patients with more competent immune systems and greater degrees of obesity may be “primed” and may generate a potentiated response or one phenotypically like that seen in older patients. Obstructive sleep apnea is a known weight-related comorbidity in patients with obesity.⁷ Poor ventilation from sleep apnea could increase atelectatic burden, explaining the increased hypoxemia and shunt fraction noted in these patients. At a younger age, this condition may not be diagnosed and may be an unknown associated risk factor. Thus, not only could obesity be an important factor in the acquisition of SARS-CoV-2 infection, obesity and obesity-related comorbidities could be important in the progression of COVID-19 after infection.

Our study has several limitations. First, this is a cross-sectional study and conducted at a single center. Though similar trends are noted in the literature,¹ a larger dataset is needed to provide more insight and explore obesity, or degree of obesity, as an individual risk factor for COVID-19 progression after controlling for other conditions, and as a function of age. We did not evaluate long-term outcomes of patients as function of age and BMI. Further study to elucidate outcomes of young patients with obesity relative to other patient populations with COVID-19 is needed. Additionally, due to the cross-sectional nature of the study, a large portion of patients were DM-unknown (no hemoglobin A1c on file and no established problem of DM). We adjusted for this in our analysis by comparing patients DM-unknown separately and found the DM-unknown subset followed a similar trend compared to other groups. Also, due to limited testing supply during the period of study, we only tested symptomatic patients in accordance with CDC guidelines. As such, some patients in the comparator group may have been SARS-CoV-2 positive. Our results are important for patients with moderate-severe symptoms of COVID-19 as defined by our study population, and thus the possible exclusion of mild or asymptomatic SARS-CoV-2 infection we felt was acceptable, especially given the low prevalence of disease at the time.

In summary, we present data suggesting younger patients hospitalized with COVID-19 were likely to have higher BMI than older patients hospitalized with COVID-19. This association was also observed in the non-DM and non-hypertension subgroups. This association does not exist in our hospitalized patients without COVID-19. Thus, we hypothesize that obesity, and particularly degree of obesity, is one significant factor driving hospitalization for COVID-19 and potentially more severe disease progression among younger individuals in Chicago that requires further epidemiologic and mechanistic studies.

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Table 1: Baseline patient characteristics

	COVID-19	No COVID-19
Diabetes Present	45/227 (20%)	30/182 (16.5%)
Diabetes Unknown	97/227 (43%)	67/182 (37%)
Hypertension Present	111/227 (49%)	63/182 (35%)
Age (years)	58.1 (56.0 – 60.2)	58.2 (55.6 – 60.8)
Male	121/227 (53%)	97/182 (53%)

	COVID-19					No COVID-19				
	Age <50 years		Age >=50 years		p	Age <50 years		Age >=50 years		p
		BMI (kg/m ²) Mean (95% CI)		BMI (kg/m ²) Mean (95% CI)			BMI (kg/m ²) Mean (95% CI)		BMI (kg/m ²) Mean (95% CI)	
No hypertension or DM	n=8	43.1 (34.5 – 51.7)	n=29	30.1 (27.7 – 32.5)	0.02	n=30	23.2 (20.1 – 26.4)	n=37	27.4 (25.5 – 29.4)	0.04
No Hypertension, DM-unknown	n=43	31.9 (29.7 – 34.1)	n=35	28.8 (26.4 – 31.2)	0.06	n=29	27.4 (24.6 – 30.1)	n=38	25.9 (23.2 – 28.6)	0.46
All patients	n=72	34.2 (32.1 – 36.3)	n=155	29.9 (28.8 – 31.0)	0.0006	n=54	27.8 (25.3 – 30.3)	n=128	28.3 (27.0 – 29.5)	0.59

Table 2: Mean BMI (95% confidence interval) comparing patients by age (<50 years vs >= 50 years) in DM and hypertension subgroups.

BMI vs Age for patients with and without COVID-19

